

Applicant : Jun-ichi Nezu et al.  
Serial No. : 10/006,611  
Filed : November 30, 2001  
Page : 2 of 14

Attorney's Docket No.: 14875-094001 / C2-103PCT-  
US

In the claims:

Please amend the claims as follows:

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Claims 1-15 (Cancelled)

Claims 16-54 (Withdrawn)

55. (New) A transgenic, non-human mammal whose genome comprises an endogenous LKB1 gene that has been genetically altered so that it can be inducibly disrupted, wherein disruption of both copies of the gene in all cells of the mammal at an embryonic stage would be lethal.

56. (New) The transgenic non-human mammal of claim 55, wherein the genetic alteration positions the LKB1 gene between a pair of recombinase target sequences.

57. (New) The transgenic, non-human mammal of claim 56, wherein the recombinase target sequences are loxP.

58. (New) The transgenic non-human mammal of claim 56, wherein the recombinase is Cre.

59. (New) The transgenic, non-human mammal of claim 56, wherein the recombinase target sequence is FRT.

60. (New) The transgenic non-human mammal of claim 56, wherein the recombinase is Flp.

Applicant : Jun-ichi Nezu et al.  
Serial No. : 10/006,611  
Filed : November 30, 2001  
Page : 3 of 14

Attorney's Docket No.: 14875-094001 / C2-103PCT-  
US

61. (New) The transgenic, non-human mammal of claim 55, wherein the mammal is a rodent.

62. (New) The transgenic, non-human mammal of claim 55, wherein the mammal is a mouse.

63. (New) The transgenic non-human mammal of claim 55, wherein the mammal is homozygous for the altered LKB1 gene.

64. (New) The transgenic non-human mammal of claim 55, wherein the mammal is heterozygous for the altered LKB1 gene.

65. (New) The transgenic non-human mammal of claim 55, wherein the mammal is a prenatal mammal.

66. (New) The transgenic non-human mammal of claim 55, wherein the mammal is a postnatal mammal.

67. (New) A transgenic, non-human mammal that is heterozygous for an engineered disruption in an LKB1 gene, wherein progeny of the transgenic non-human animal that are homozygous for the engineered disruption have a phenotype of embryonic lethal.

Applicant : Jun-ichi Nezu et al.  
Serial No. : 10/006,611  
Filed : November 30, 2001  
Page : 4 of 14

Attorney's Docket No.: 14875-094001 / C2-103PCT-  
US

68. (New) The transgenic non-human mammal of claim 67, wherein the transgenic, non-human mammal develops polyposis postnatally in its digestive tract or pigmental spot formation on mucous membrane or skin.

69. (New) The transgenic, non-human mammal of claim 67, wherein the LKB1 gene is positioned between a pair of recombinase target sequences.

70. (New) The transgenic, non-human mammal of claim 69, wherein the recombinase target sequence is loxP.

71. (New) The transgenic, non-human mammal of claim 69, wherein the recombinase is Cre.

72. (New) The transgenic, non-human mammal of claim 69, wherein the recombinase target sequence is FRT.

73. (New) The transgenic, non-human mammal of claim 69, wherein the recombinase is Flp.

74. (New) The transgenic, non-human mammal of claim 67, wherein the mammal is a rodent.

75. (New) The transgenic, non-human mammal of claim 67, wherein the rodent is a mouse.

Applicant : Jun-ichi Nezu et al.  
Serial No. : 10/006,611  
Filed : November 30, 2001  
Page : 5 of 14

Attorney's Docket No.: 14875-094001 / C2-103PCT-  
US

76. (New) A transgenic, non-human prenatal mammal in which both alleles of a LKB1 gene are disrupted, wherein the mammal shows a phenotype of embryonic lethal.

77. (New) The transgenic, non-human mammal of claim 76, wherein both alleles of the LKB1 gene in the mammal or an ancestor of the mammal was positioned between a pair of recombinase target sequences.

78. (New) The transgenic, non-human mammal of claim 77, wherein the recombinase target sequence is loxP.

79. (New) The transgenic, non-human mammal of claim 77, wherein the recombinase is Cre.

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80. (New) The transgenic, non-human mammal of claim 77, wherein the recombinase target sequence is FRT.

81. (New) The transgenic non-human mammal of claim 77, wherein the recombinase is Flp.

82. (New) The transgenic, non-human mammal of claim 76, wherein the mammal is a rodent.

83. (New) The transgenic, non-human mammal of claim 76, wherein the rodent is a mouse.

Applicant : Jun-ichi Nezu et al.  
Serial No. : 10/006,611  
Filed : November 30, 2001  
Page : 6 of 14

Attorney's Docket No.: 14875-094001 / C2-103PCT-  
US

84. (New) A transgenic, non-human, postnatal mammal, wherein an endogenous LKB1 gene or a portion or regulatory region thereof, positioned between a pair of target sequences of a recombinase, has been disrupted postnatally mammal by the recombinase-mediated deletion of the endogenous LKB1 gene, wherein the mammal exhibits digestive tract polyposis or pigmental spot formation on mucous membrane or skin.

85. (New) The transgenic non-human animal of claim 84, wherein the disruption is in a transcribed region of the LKB1 gene.

86. (New) The transgenic non-human animal of claim 84, wherein the disruption is in a regulatory region of the LKB1 gene.

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87. (New) The transgenic, non-human mammal of claim 84, wherein the recombinase target sequence is loxP.

88. (New) The transgenic, non-human mammal of claim 84, wherein the recombinase is Cre.

89. (New) The transgenic, non-human mammal of claim 84, wherein the recombinase target sequence is FRT.

90. (New) The transgenic, non-human mammal of claim 84, wherein the recombinase is Flp.

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Applicant : Jun-ichi Nezu et al.  
Serial No. : 10/006,611  
Filed : November 30, 2001  
Page : 7 of 14

Attorney's Docket No.: 14875-094001 / C2-103PCT-  
US

91. (New) The transgenic, non-human mammal of claim 84, wherein the mammal is a rodent.

92. (New) The transgenic, non-human mammal of claim 84, wherein the mammal is a mouse.